PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PU4783WO	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US 03/32473	International filing date *(day/month/year)* 14.10.2003	Priority date *(day/month/year)* 15.10.2002
International Patent Classification (IPC) or both national classification and IPC C07D487/04		
Applicant SMITHKLINE BEECHAM CORPORATION		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
15.04.2004	24.01.2005
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Baston, E Telephone No. +49 89 2399-8229

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US 03/32473

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-121 as originally filed

Claims, Numbers

1-25 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 8,15,19,20,24,25 "with respect to industrial applicability"

   because:

   ☒ the said international application, or the said claims Nos. 8,15,19,20,24,25 relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-25
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-25
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-7,9-14,16-18,21-23
	No:	Claims	

2. Citations and explanations

   see separate sheet

To section III

Claims 8,15,19,20,24,25 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

To section V

The following documents were cited in the search report and were considered for the examination of the present application:

D1: WO 03 051886; D2: WO 03 080616; D3: WO 03 068773;
D4: WO 02 18346

The priority document of the present application is not yet available. In case that the presently claimed subject matter is not fully supported by the priority document, D1-D3 might be relevant for the assessment of novelty and / or inventive step in the national / European phase. At present it is considered that specially D1 is highly relevant for assessing novelty of claims 8-15 and 18-22.

The present application relates to 3-substituted derivatives of pyradazin, which are considered to be useful for the treatment of diabetes due to inhibition of glycogen synthase kinase (GSK3). The compounds are characterized by the presence of either a pyridyl or a pyrimidyl group in position 3 (claims 1-7). Furthermore the application relates to a method for the treatment using compounds according to claim 8, which are defined broader and also encompass structures known from D1.

The prior art D4 relates to pyrazole derivatives which are not condensed (also kinase inhibition, but different application); due to this structural difference this document is not relevant for the assessment of novelty and inventive step. The application thus meets the requirements of Art. 33(2)(3) PCT in the light of D4.

The application only contains examples for compounds with D=N, but not for D= CH and thus the requirements of Art. 6 PCT are not met.

Claim 8 is not clear (Art. 6 PCT), since the expression "disorder being characterized by misregulation of GSK-3" is not suitable to specifiy for which subject-matter protection

might be sought.
Claim 8 refers to formula (I), which is different from formula (I) of claim 1; consequently a different number has to be attributed for the formula of claim 8.
Claims 9-14 are not clear, since they refer to claims of a different category.

Claim 19 is not clear due to the expression "disorder being mediated by inappropriate GSK-3 activity".
The Applicant should bear in mind, that the affinity for a specific enzyme cannot be claimed, but needs to be replaced by a specific pathological condition.

For the assessment of the present claims 8,15,19,20,24,25 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.